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学位論文題名	Characterization of two Lemur kinase 1 (LMTK1) isoforms, the similarity and difference 脳の新規キナーゼ Lemur kinase 1 (LMTK1) の 2 つのアイソフォームの性質と機能に関する研究（英文）
論文審査委員	主査　准教授　安藤　香奈絵 委員　教　授　岡本　龍史 委員　教　授　川原　裕之 委員　客員教授　久永　眞市

【論文の内容の要旨】

Lemur Kinase 1 (LMTK1) is a Ser/Thr kinase expressed mainly in neurons. We recently reported that LMTK1A regulates outgrowth of axons and dendrites using cultured primary neurons. However, there is another isoform LMTK1B in LMTK1. LMTK1A and LMTK1B are alternative splicing isoforms; the non-transmembrane type A (LMTK1A) and transmembrane type B (LMTK1B). While LMTK1B is an integral membrane protein with transmembrane sequences at the N-terminal region, LMTK1A binds to membrane through palmitoylation at three cysteine residues in the N-terminal region. Considering that the outgrowth of axons and dendrites is critical for neuronal circuit formation, it is important to determine whether LMTK1B has a similar function. It is also interesting to know if they have isoform-specific function. Firstly, we analyzed expression of LMTK1A and LMTK1B in mouse brain. qPCR revealed similar expression levels of LMTK1A and LMTK1B, and their expression was increased with brain development. The cellular localization of LMTK1A and LMTK1B was observed in cultured cells and primary neurons after transfection. A wild type of two isoforms showed a similar cellular distribution at the perinuclear region with Rab11a. By contrast, kinase negative (kn) mutants displayed the different cellular localization, LMTK1A kn distributed diffusely in the whole cytoplasm whereas LMTK1B kn

exhibited tubular distribution similar to ER around the nucleus. We found the different effects of kn mutants on axon outgrowth and dendritic spine formation.